Remarks

Applicants request reconsideration on the merits of the above-referenced patent application.

I. Claim amendments

Claims 6-28 are pending. This amendment amends only claims 21 and 28. These amendments correct obvious typographical errors, and are, therefore, permissible under MPEP §2163.07.

Applicants request that the amendments be entered because they only require a cursory review, and reduce the issues on appeal. In addition, Applicants respectfully submit that the amendment to claim 28 should be added as a matter of right, given that it complies with the suggested language in the June 1, 2007 Office action. *See* MPEP §§714.12 & 714.13.

Applicants reserve the right to pursue any canceled subject matter and/or any other subject matter disclosed in this application in one or more divisional and/or continuation applications.

II. Response to the double patenting rejections

Claims 6-11 and 17-20 have been rejected under the judicially-created doctrine of obviousness-type double patenting in view of claims 1-4 of US Patent 6,682,745. Applicants request withdrawal of this rejection. Applicants have enclosed a terminal disclaimer citing US Patent 6,682,745. Thus, this rejection is moot. Applicants are submitting the terminal disclaimer to expedite prosecution of this patent application. Applicants make no representation as to the merits of this rejection.

Claims 6-8 have been rejected under the judicially-created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of US Patent 6,120,775. Applicants request withdrawal of this rejection. Applicants have enclosed a terminal disclaimer citing US Patent 6,120,775. Thus, this rejection is moot. Applicants are submitting the terminal disclaimer to expedite prosecution of this patent application. Applicants make no representation as to the merits of this rejection.

III. Response to objection to claim 28

An objection has been raised to claim 28 for depending from a canceled claim. Applicants request withdrawal of this objection. Claim 28 has been amended to depend from claim 21 rather than claim 1, as suggested by the Office action. Thus, this objection is moot. Applicants thank the Examiner for identifying this typographical error.

IV. Response to new matter rejection

Claims 21-28 have been rejected under 35 U.S.C. §112 (first paragraph) for including new matter. More specifically, the claims have been rejected for reciting a method for *systemic* application of live attenuated bacteria. Applicants request withdrawal of this rejection.

Applicants respectfully submit that their specification supports claims directed to a method for systemic application of live attenuated bacteria. For example, Applicants' specification states:

> **This invention is widely applicable in the field of manufacture of *systemic* vaccines.** It is not restricted to any specific bacterium or a specific disease. **Practically all live attenuated bacteria that are suitable for the manufacture of a live attenuated vaccine for systemic application are equally suitable for use in this specific invention.** Systemic application comprises all applications in which the vaccine is not applied to the mucosa (mucosal application comprises i.a. oral and intranasal vaccination)... Therefore this embodiment of the invention relates to the use of live attenuated bacteria for the manufacture of a vaccine for submucosal administration. Mucosal tissue is found i.a. in the mouth, the nose, the lining of the gut, the eye, the vulva and the lips... Submucosal application is understood to be administration through the upper layer of the mucosa, and into the submucosa. Applicants' specification, pages 1, line 25 to page 3, line 4 (emphasis added).

The results in Example 1 on page 7-8 also provide support. That example illustrates the use of submucosal administration of two different live attenuated bacterial strains, and reports systemic protection following vaccination:

> After challenge, the five horses vaccinated submucosally with the TW 928 deletion mutant appeared completely protected. Complete protection was also obtained in the horses vaccinated intramuscularly with the TW 928 deletion mutant.... Therefore it can be concluded that ... full protection can be obtained with suitable vaccine strains regardless the site of administration; intramuscularly or submucosally. Applicants' specification, page 8, lines 12-17.

In view of the foregoing, Applicants respectfully submit that the new matter rejection should be withdrawn.

V. Response to written description rejection based on failure to show possession of entire scope of invention

Claims 6-28 have been rejected under 35 U.S.C. §112 (first paragraph) for lacking written description support in the specification. Applicants request withdrawal of this rejection. In support of this request, Applicants state the following:

A. Claim 6

Claim 6 is directed to a method for administering a live attenuated vaccine to a mammal. The method comprises injecting an immunogenically effective amount of the vaccine into a submucosal layer of the mammal.

This method stems from Applicants' discovery that submucosal administration of live attenuated vaccines generally tends to reduce local adverse reactions that had previously been observed when such vaccines were administered via conventional routes for systemic application (particularly intramuscular administration). This reduction in local reactions is advantageous because it, for example, generally allows for less-attenuated vaccines to be used. *See e.g.*, Applicants' specification, page 1, lines 20-24. Applicants' discovery is not limited to any specific live attenuated vaccine. To the contrary, **Applicants' discovery is generally applicable to *all* live attenuated vaccines, independent of the bacterial strain or method of attenuation.** *See, e.g.*, Applicants' specification, page 1, lines 25-28. This is corroborated by Examples 1-3 in Applicants' specification on pages 7-9, which illustrate the reduction of local reactions by using submucosal administration with **four different live bacterial strains** and **two different animal species**.

Applicants' specification provides direction and guidance for practicing the invention. For example, Applicants' specification provides generally suitable sites for submucosal administration (*see, e.g.*, page 2, line 30 to page 3, line 2 and page 3, lines 18-23); administration depths and techniques (*see, e.g.*, page 3, lines 3-17); dosage ranges (*see, e.g.*, page 6, lines 1-8); suitable carrier materials (*see, e.g.*, page 6, lines 9-17); and suitable adjuvants (*see, e.g.*, page 6, lines 18-26). Applicants' specification also, for example, specifically identifies a range of live

bacteria that are generally suitable for use with their invention. *See, e.g.*, page 3, line 25 to page 5, line 29. And, as noted above, Applicants' specification provides three working examples illustrating submucosal administration with four different live vaccines and two different host species. *See* Examples 1-3, pages 7-9.

The Office action rejects claim 6 under 35 U.S.C. §112 (first paragraph) for not having sufficient written description in the specification to support the general applicability of the recited method to all live attenuated bacterial vaccines. Applicants respectfully request reconsideration of this conclusion. Applicants agree with the rule set forth in the Office action that the specification must describe the entire scope of the claims in such detail that would have reasonably conveyed to a skilled artisan that Applicants had possession of the claimed invention. Applicants also agree that possession of an invention may be shown by: (a) actual reduction to practice, (b) a clear depiction of the invention in a detailed drawing, or (c) a description providing sufficient relevant (*i.e.*, distinguishing) identifying characteristics of the invention. Applicants, however, respectfully submit that their specification provides sufficient distinguishing identifying characteristics of the invention.

The law is clear that Applicants' specification must provide a detailed description for only the *novel* aspects of their invention. *See, e.g., Third Wave Tech. v. Stratagene Corp.*, 405 F.Supp.2d 991, 1002 (W.D. Wis. 2005), citing *Genetech v. Novo Nordisk* A/S, 108 F.3d 1361, 1366, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997). *See also, Falkner v. Inglis*, 448, F.3d 1357, 1368, 79 USPQ2d 1001, 1008 (Fed. Cir. 2006) (a requirement that patentees recite known DNA structures would serve no goal of the written description requirement). **In fact, the Federal Circuit discourages inclusion of information that is well-known in the art.** *See, e.g., Hybritech v. Monoclonal Antibodies*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986) (a patent *preferably omits* anything that is well-known in the art). Applicants, therefore, should not be penalized for omitting such information.

In claim 6, the *novel* aspect of Applicants' invention is submucosal administration. It is undisputed that Applicants' specification provides a sufficient description of this. The written description rejection, instead, is directed to the recitation of a live attenuated bacterial vaccine. Specifically, the rejection indicates that the specification is insufficient to support the scope of claim 6 because the specification fails to describe how to attenuate bacteria other than

Streptococcus equi. Applicants respectfully submit that this rejection is contrary to the law.

Live attenuated bacterial vaccines, as a general class, were not novel at the time of Applicants' filing. To the contrary, many such vaccines and methods for their preparation were well-known. To evidence this, **Table I** provides a long list of references discussing live attenuated vaccines and their preparation:

Table I
Examples of Live Attenuated Vaccines Known at the Time of Applicants' Filing[1]

Live vaccine	Reference	Filing date (if applicable)	Publication date
Actinobacillus pleuropneumoniae	Inzana, T.J., US Patent 5,429,818, entitled "Non-capsulated mutants of *Actinobacillus pleuropneumoniae* useful as vaccines"	Priority: December 6, 1991 Filed: June 24, 1993	July 4, 1995
Actinobacillus pleuropneumoniae	Segers, R.P.A.M., et al., US Patent 6,013,266, entitled "Live attenuated bacteria of the species *Actinobacillus pleuropneumoniae*"	Priority: April 10, 1997 Filed: April 9, 1998	January 11, 2000
Actinobacillus pleuropneumoniae	Fuller, T.E., et al., US Patent 5,925,354, entitled "Riboflavin mutants as vaccines against *Actinobacillus pleuropneumoniae*"	Priority: November 30, 1995 Filed: October 28, 1996	July 20, 1999
Bordetella bronchiseptica	Switzer, W.P., et al, US Patent 4,225,583, entitled "Intra-respiratory vaccine for prevention of *Bordetella bronchiseptica* infection and method of use"	December 7, 1978	September 30, 1980

[1] These references, which the Undersigned located during a *non-exhaustive* search, have already been cited and enclosed with Applicants' June 22, 2006 Amendment D.

Live vaccine	**Reference**	**Filing date (if applicable)**	**Publication date**
Brucella abortus	Adams, L.G., US Patent 5,718,903, entitled "Vaccine comprising *Brucella abortus* which has O polysaccharide antigen absent"	Priority: March 30, 1987 Filed: February 14, 1994	February 17, 1998
Brucella abortus	McEwen, A.D., et al., "Bovine contagious abortion. The use of guinea-pigs in immunisation studies," *The Journal of Comparative Pathology and Therapeutics*, XLIX(2), 97-117 (June 30, 1036)	N/A	June 30, 1936
Clostridium perfringens	Segers, R.P.A.M., et al., US Patent 6,610,300, entitled "*Clostridium perfringens* vaccine"	Priority: June 20, 1997 Filed: June 19, 1998	August 26, 2003
Corynebacterium pseudotuberculosis	Simmons, C.P., "Attenuation and vaccine potential of *aroQ* mutants of *Corynebacterium pseudotuberculosis*," *Infection and Immunity*, 65(8), pp. 3048-3056 (August, 1997)	N/A	August of 1997
Escherichia coli, *Salmonella typhimurium*, & *Shigella flexneri*	Powell, R.J., et al., US Patent 5,997,881, entitled "Method of making non-pyrogenic lipopolysaccharide or A"	Purported priority: November 22, 1995 Filed: February 19, 1997	December 7, 1999
Erysipelothrix rhusiopathiae	Sakano, T., et al., "Effect of attenuated *Erysipelothrix rhusiopathiae* vaccine in pigs infected with porcine reproductive respiratory syndrome virus," *Journal of Veterinary Medical Science*, 59(11), pp. 977-981 (November, 1997)	N/A	November of 1997

Live vaccine	Reference	Filing date (if applicable)	Publication date
Erysipelothrix rhusiopathiae	Sawada, T., et al., "Cross protection of mice and swine inoculated with culture filtrate of attenuated *Erysipelothrix rhusiopathiae* and challenge exposed to strains of various serovars," *American Journal of Veterinary Research*, 48(2), pp. 239-242 (February, 1987)	N/A	February of 1987
Mycobacterium bovis	Flesselles, B., et al., US Patent 6,136,324, entitled "Attenuated strains of mycobacteria"	August 21, 1997	October 24, 2000
Mycobacterium bovis	Barry, III, C.E., et al., US Patent 6,403,100, entitled "Method of attenuating pathogenic mycobacteria and strains of mycobacteria so attenuated"	Priority: July 10, 1997 Filed: July 9, 1998	Appl. published: January 21, 1999 Issued: June 11, 2002
Pasteurella haemolytica	Kucera, C.J., US Patent 4,506,017, entitled "Modified *Pasteurella haemolytica* bacteria"	Priority: April 17, 1981 Filed: January 19, 1983	March 19, 1985
Pasteurella multocida	Maheswaran, S.K., US Patent 3,855,408, entitled "Poultry vaccine"	July 16, 1973	December 17, 1974
Pasteurella multocida	Glisson, J.R., et al., US Patent 4,999,191, entitled "*Pasteurella multocida* Vaccine"	May 5, 1988	March 12, 1991
Rhodococcus equi	Chirino-Trejo, J.M., et al., "Protection of foals against experimental *Rhodococcus equi* pneumonia by oral immunization," *Canadian Journal of Veterinary Research*, 51, pp. 444-447 (1987)	N/A	1987

Live vaccine	Reference	Filing date (if applicable)	Publication date
Salmonella choleraesuis	Smith, H.W., US Patent 3,364,117, entitled "Vaccine for combating *Salmonella choleraesuis* infection"	Priority: September 10, 1963 Filed: September 9, 1964	January 16, 1968
Salmonella dublin & *Salmonella typhimurium*	Stocker, B.A.D., US Patent 4,550,081, entitled "Non-reverting salmonella"	Priority: May 19, 1980 Filed: September 7, 1982	October 29, 1985
Staphylococcus aureus	Australian Patent Appl. AU198285929A1, entitled "Mastitis vaccine"	July 12, 1982	January 20, 1983
Streptococcus pneumoniae	Helms, C.M., "Temperature-sensitive mutants of type I *Streptococcus pneumoniae*: preparation, characterization, and evidence for attenuation and immunogenicity," *The Journal of Infectious Diseases*, 136 (Supp.), pp. S208-S215 (August, 1977)	N/A	August of 1977
Streptococcus suis	Quessy, S., et al., "Immunization of mice against *Streptococcus suis* serotype 2 infections using a live avirulent strain," *Canadian Journal of Veterinary Research (Short Communications)*, 58, pp. 299-301 (1994)	N/A	1994
Streptococcus suis	Busque, P., et al., "Immunization of pigs against *Streptococcus suis* serotype 2 infection using a live avirulent strain," *Canadian Journal of Veterinary Research*, 61, pp. 275-279 (1997)	N/A	1997

The references in **Table I** are all dated before or near the time of Applicants' July 29, 1997 priority date, and, therefore, demonstrate that a plethora of representative live attenuated bacterial vaccines existed in the art at the time of Applicants' filing. Adding to this abundance of knowledge, Applicants' specification specifically identifies a range of live attenuated bacteria that are generally suitable for use with their invention (*see* page 3, line 25 to page 5, line 29), as well as three working examples illustrating benefits of submucosal administration with four different live vaccines and two different host species (*see* Examples 1-3, pages 7-9). **Applicants, therefore, respectfully submit that their specification --- when viewed in the context of the art at the time of applicants filing --- satisfies the written description requirement with respect to claim 6. Such a conclusion accords with the Federal Circuit's holding in *Falkner*:**

> [W]here, as in this case, accessible literature sources clearly provided, as of the relevant date, genes and their nucleotide sequences (here "essential genes"), satisfaction of the written description requirement does not require either the recitation or incorporation by reference (where permitted) of such genes and sequences. *Falkner*, 448, F.3d at 1368, 79 USPQ2d at 1008-1009 (footnote omitted).

As a final note, the written description rejection seems to suggest that attenuation of bacteria requires that the bacteria be usable in a vaccine "without any adverse reaction." *See* June 1, 2007 Office action, page 5, lines 17-20. Applicants respectfully submit that this may stem from a misunderstanding of the term "attenuated" as used in claim 6. The attenuated bacteria recited in claim 6 can have an adverse reaction when used in a vaccine. In fact, such a vaccine *likely will* have an adverse reaction when administered via at least some routes (*e.g.*, intramuscularly). After all, a primary purpose of Applicants' invention is to reduce adverse reactions associated with live attenuated vaccines. This is repeatedly discussed by Applicants' specification. For example, at lines 9-16 on page 2, Applicants' specification states:

> [M]any bacterial IM administered vaccines cause large abscesses at the site of injection. These abscesses may stay there from days to months. In those cases in which a live attenuated bacterium must behave relatively virulent in order to trigger an adequate immune response, the bacterium often replicates at the injection site to such a level that the abscess even bursts. Large intramuscular or skin-abscesses are clearly an unacceptable side-effect of vaccination with bacterial live attenuated strains, but

> unavoidable if further attenuation spoils the immunogenic potential of the bacterium. This causes the dilemma mentioned above, for which the invention offers a solution.

Moreover, even the live attenuated bacterial vaccine exemplified in Example 1 on page 7-8 of Applicants' specification causes adverse effects, particularly when administered intramuscularly. Simply put, the method of claim 6 can generally be used with any live attenuated vaccine, and is particularly useful with vaccines that cause adverse reactions when administered systemically via a non-submucosal route. Applicants, therefore, respectfully submit that their specification can satisfy the written description requirement without describing how to prepare a live attenuated bacterial vaccine having an absence of adverse reactions.

B. *Claims 7, 8, and 12-19*

Claims 7, 8, and 12-19 depend directly or indirectly from claim 6. Like claim 6, claims 7, 8, and 12-19 have been rejected for not having sufficient written description in the specification to support the scope of live attenuated bacterial vaccines recited in the claims. Applicants respectfully submit that these claims are supported for at least the same reasons as claim 6.

C. *Claim 9*

Claim 9 is directed to a method for reducing adverse reactions in a mammal at an injection site of a live attenuated bacterial vaccine. The vaccine comprises bacteria that cause abscess formation when administered intramuscularly. The method comprises administering the vaccine submucosally. The reduction of adverse reactions is measured by the amount or size of abscesses or lesions at the mucosal injection site compared to an intramuscular injection site.

Like claim 6, claim 9 has been rejected for not having sufficient to written description in the specification for live attenuated bacteria other than *Streptococcus equi*. Applicants respectfully submit that claim 9 is supported for at least the same reasons as claim 6.

D. *Claims 10, 11, and 20*

Claims 10, 11, and 20 depend from claim 9. Like claim 9, claims 10, 11, and 20 have been rejected for not having sufficient written description in the specification to support the

scope of live attenuated bacterial vaccines recited in the claims. Applicants respectfully submit that these claims are supported for at least the same reasons as claim 9.

E. *Claim 21*

Claim 21 is directed to a method for systemic application of live attenuated bacteria to a mammal. The bacteria cause abscess and/or lesion formation in the mammal if they are administered intramuscularly or intradermally to the mammal. The method comprises administering the bacteria submucosally to the mammal. Any abscess and/or lesion formation at the site of the submucosal administration is less in total size than the abscess and/or lesion formation that would occur if the bacteria are instead administered intramuscularly or intradermally to the mammal.

Like claim 6, claim 21 has been rejected for not having sufficient to written description in the specification for live attenuated bacteria other than *Streptococcus equi*. Applicants respectfully submit that claim 21 is supported for at least the same reasons as claim 6.

F. *Claims 22-28*

Claims 22-28 depend from claim 21. Like claim 21, claims 22-28 have been rejected for not having sufficient written description in the specification to support the scope of live attenuated bacterial vaccines recited in the claims. Applicants respectfully submit that these claims are supported for at least the same reasons as claim 21.

VI. Response to the enablement rejection

Claims 6-28 have been rejected under 35 U.S.C. §112 (first paragraph) for lacking enablement commensurate to the breadth of the claims. Specifically, the Office action indicates that Applicants' specification is not enabling for live attenuated bacteria other than *Streptococcus equi*. Applicants request withdrawal of this rejection. In support of this request, Applicants state the following:

A. *Claim 6*

Claim 6 is directed to a method for administering a live attenuated vaccine to a mammal. The method comprises injecting an immunogenically effective amount of the vaccine into a submucosal layer of the mammal. As noted above, this method stems from Applicants' discovery that submucosal administration of live attenuated vaccines generally tends to reduce local adverse reactions that had previously been observed when such vaccines were administered via conventional routes. Applicants' discovery is not limited to any specific live attenuated vaccine. To the contrary, Applicants' discovery is generally applicable to *all* live attenuated vaccines, independent of the bacterial strain or method of attenuation. This is corroborated by Examples 1-3 in Applicants' specification, which illustrate the reduction of local reactions by using submucosal administration with four different live bacterial strains and two different animal species.

The enablement rejection indicates that the specification is insufficient to enable the scope of claim 6 because the specification fails to describe how to make and use live attenuated bacterial strains other than *Streptococcus equi*. Applicants respectfully request reconsideration of this conclusion. A claim satisfies the enablement requirement if the specification enables a skilled artisan to make and use the claimed invention without "undue experimentation." The necessity for "complex" experimentation does not necessarily equate to "undue" experimentation if those in the art typically engage in such experimentation. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). *See also,* MPEP §2164.01. Claims are enabled even if "a considerable amount" of experimentation is necessary where the experimentation is "merely routine" or the specification "provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. Whether a specification requires undue experimentation depends on multiple factors:

> (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Wands*, 858 F.2d at 737, 8 USPQ2d at 1404.

See also, MPEP §2164.01(a).

Applicants submit that their claims satisfy the enablement requirement for reasons analogous to those in *Wands*. More specifically, in *Wands*, the claims were directed to monoclonal IgM antibodies and an immunoassay using the antibodies. The court found that the claims were enabled even though a skilled artisan practicing the claimed invention would have to obtain lymphocytes from an immunized animal; fuse the lymphocytes with myeloma cells; and then perform multiple screening steps to identify and separate out hybridomas, hybridomas producing antibodies to the desired antigen, and finally hybridomas producing antibodies having the claimed affinity. *Wands*, 858 F.2d at 739-740, 8 USPQ2d at 1404-1406. In finding enablement, the court noted: (1) the specification provided guidance for practicing the invention, (2) the specification provided working examples, (3) the level of skill in the art was high, (4) the methods needed to practice the invention were well known in the art, and (5) the nature of the technology involved screening to identify antibodies with the desired characteristics. *Wands*, 858 F.2d at 740, 8 USPQ2d at 1406. **Using reasoning analogous to *Wands*, Applicants' claim 6 also should be found to satisfy the enablement requirement. Specifically:**

1. **Applicants' specification provides guidance for practicing the invention.** For example, Applicants' specification provides generally suitable sites for submucosal administration, administration depths and techniques, dosage ranges, suitable carrier materials, and suitable adjuvants. Applicants' specification also identifies a wide range of live bacteria that are generally suitable for use with their invention.

2. **Applicants' specification provides three working examples illustrating submucosal administration with four different live vaccines and two different host species.** These examples include two different live attenuated bacterial strains.

3. **The skill level in the art and nature of the technology are analogous to those in *Wands*.**

4. **The methods needed to practice the invention are well known in the art.** As to live attenuated vaccines in particular, there was an extensive understanding in the art relating to methods for making and generally using live vaccines at the time Applicants filed their application. The scientific literature from the time of Applicants' filing is replete with discussions relating to the development and use of live attenuated vaccines. The non-exhaustive list of references cited in the above **Table I** demonstrates this.

A finding of enablement is further supported by the Federal Circuit's holding in *Falkner*. In that case, the court found that the Board did not err in finding enablement for a poxvirus vaccine claim, even in the absence of a poxvirus working example, where there was a working example for a herpesvirus vaccine. *Falkner*, 448 F.3d at 1365, 79 USPQ2d at 1006. In justifying its holding, the court acknowledged that "great expenditures of time and effort were ordinary in the field of vaccine preparation." *Id.*

Simply put, Applicants specification --- when viewed in the context of the knowledge in the art at the time of applicants filing --- enables claim 6. Accordingly, Applicants respectfully submit that the enablement rejection of claim 6 should be withdrawn.

B. *Claims 7, 8, and 12-19*

Claims 7, 8, and 12-19 depend directly or indirectly from claim 6. Like claim 6, claims 7, 8, and 12-19 have been rejected for not having sufficient description in the specification to enable the scope of live attenuated bacterial vaccines recited in the claims. Applicants respectfully submit that these claims are enabled for at least the same reasons as claim 6.

C. *Claim 9*

Claim 9 is directed to a method for reducing the amount of adverse reactions in a mammal at an injection site of a live attenuated bacterial vaccine. The vaccine comprises bacteria that cause abscess formation when administered intramuscularly. The method comprises administering the vaccine submucosally. The reduction of adverse reactions is measured by the amount or size of abscesses or lesions at the mucosal injection site compared to an intramuscular injection site.

Like claim 6, claim 9 has been rejected for not enabling the use of live attenuated bacteria other than *Streptococcus equi*. Applicants respectfully submit that claim 9 is enabled for at least the same reasons as claim 6.

D. *Claims 10, 11, and 20*

Claims 10, 11, and 20 depend from claim 9. Like claim 9, claims 10, 11, and 20 have been rejected for not having sufficient description in the specification to enable the scope of live attenuated bacterial vaccines recited in the claims. Applicants respectfully submit that these claims are enabled for at least the same reasons as claim 9.

E. *Claim 21*

Claim 21 is directed to a method for systemic application of live attenuated bacteria to a mammal. The bacteria cause abscess and/or lesion formation in the mammal if they are administered intramuscularly or intradermally to the mammal. The method comprises administering the bacteria submucosally to the mammal. Any abscess and/or lesion formation at the site of the submucosal administration is less in total size than the abscess and/or lesion formation that would occur if the bacteria are instead administered intramuscularly or intradermally to the mammal.

Like claim 6, claim 21 has been rejected for not enabling the use of live attenuated bacteria other than *Streptococcus equi*. Applicants respectfully submit that claim 21 is enabled for at least the same reasons as claim 6.

F. *Claims 22-28*

Claims 22-28 depend from claim 21. Like claim 21, claims 22-28 have been rejected for not having sufficient description in the specification to enable the scope of live attenuated bacterial vaccines recited in the claims. Applicants respectfully submit that these claims are enabled for at least the same reasons as claim 21.

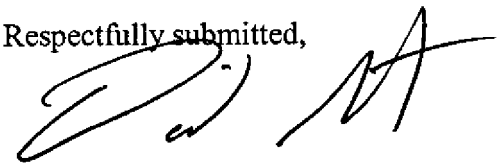
* * * * * * * * *

Applicants hereby request a two-month extension to respond to the June 1, 2007 Office action, and authorize the Commissioner to charge Deposit Account No. **02-2334** for the corresponding extension fee. Applicants also authorize the Commissioner to charge Deposit Account No. **02-2334** for the fees corresponding to the two enclosed terminal disclaimers. Finally, Applicants are submitting a notice of appeal in parallel with this Amendment F, and authorize

the Commissioner to charge Deposit Account No. **02-2334** for the corresponding fee for that notice. Applicants do not believe that they owe any other fee in connection with this filing. If, however, Applicants do owe any such fee(s), the Commissioner is hereby authorized to charge the fee(s) to Deposit Account No. **02-2334**. In addition, if there is ever any other fee deficiency or overpayment under 37 C.F.R. §1.16 or 1.17 in connection with this patent application, the Commissioner is hereby authorized to charge such deficiency or overpayment to Deposit Account No. **02-2334**.

Applicants submit that the pending claims are in condition for allowance, and request that this application be allowed. The Examiner is requested to call the Undersigned if any issues arise that can be addressed over the phone to expedite examination of this application.

Respectfully submitted,



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